#3

DATE: 10/30/2001

TIME: 11:59:43

OIPE

```
Input Set : A:\Rih32d31.app
                    Output Set: N:\CRF3\10302001\I903063.raw
     3 <110> APPLICANT: Wands, Jack R.
             de la Monte, Suzanne M.
      5
             Ince, Nedim
             Carlson, Rolf I.
     8 <120> TITLE OF INVENTION: DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS
    10 <130> FILE REFERENCE: 21486-032 DIV3
    12 <140> CURRENT APPLICATION NUMBER: 09/903,063
C--> 13 <141> CURRENT FILING DATE: 2001-10-11
    15 <150> PRIOR APPLICATION NUMBER: 09/436,184
                                                               ENTERED
    16 <151> PRIOR FILING DATE: 1999-11-08
    18 <160> NUMBER OF SEQ ID NOS: 9
    20 <170> SOFTWARE: PatentIn Ver. 2.1
     22 <210> SEQ ID NO: 1
     23 <211> LENGTH: 36
     24 <212> TYPE: PRT
     25 <213> ORGANISM: Artificial Sequence
     27 <220> FEATURE:
     28 <223> OTHER INFORMATION: Description of Artificial Sequence: Consensus
              EGF-like domain
     31 <220> FEATURE:
     32 <221> NAME/KEY: VARIANT
     33 <222> LOCATION: (2)..(8)
     34 <223> OTHER INFORMATION: Wherein Xaa is any amino acid
     36 <220> FEATURE:
     37 <221> NAME/KEY: VARIANT
     38 <222> LOCATION: (10)..(13)
     39 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     41 <220> FEATURE:
     42 <221> NAME/KEY: VARIANT
     43 <222> LOCATION: (15)..(24)
     44 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     46 <220> FEATURE:
     47 <221> NAME/KEY: VARIANT
     48 <222> LOCATION: (26)
     49 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     51 <220> FEATURE:
     52 <221> NAME/KEY: VARIANT
     53 <222> LOCATION: (28)..(35)
     54 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     56 <400> SEQUENCE: 1
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     58
         1
                                        Cys Kaa Cys Xaa Xaa Xaa Xaa Xaa
W--> 60 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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                     20
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     64
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     67 <210> SEQ ID NO: 2
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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/903,063

Input Set : A:\Rih32d31.app

Output Set: N:\CRF3\10302001\1903063.raw

68 <211> LENGTH: 758 69 <212> TYPE: PRT 70 <213> ORGANISM: Homo sapiens 72 <400> SEQUENCE: 2 73 Met Ala Gln Arg Lys Asn Ala Lys Ser Ser Gly Asn Ser Ser Ser Ser 5 76 Gly Ser Gly Ser Gly Ser Thr Ser Ala Gly Ser Ser Fro Gly Ala 25 79 Arg Arg Glu Thr Lys His Gly Gly His Lys Asn Gly Arg Lys Gly Gly 40 82 Leu Ser Gly Thr Ser Phe Phe Thr Trp Phe Met Val Ile Ala Leu Leu 55 85 Gly Val Trp Thr Ser Val Ala Val Val Trp Phe Asp Leu Val Asp Tyr 88 Glu Glu Val Leu Gly Lys Leu Gly Ile Tyr Asp Ala Asp Gly Asp Gly 91 Asp Phe Asp Val Asp Asp Ala Lys Val Leu Leu Gly Leu Lys Glu Arg 105 100 94 Ser Thr Ser Glu Pro Ala Val Pro Pro Glu Glu Ala Glu Pro His Thr 120 97 Glu Pro Glu Glu Gln Val Pro Val Glu Ala Glu Pro Gln Asn Ile Glu 135 140 100 Asp Glu Ala Lys Glu Gln Ile Gln Ser Leu Leu His Glu Met Val His 150 155 103 Ala Glu His Val Glu Gly Glu Asp Leu Gln Glu Asp Gly Pro Thr 165 170 106 Gly Glu Pro Gln Gln Glu Asp Asp Glu Phe Leu Met Ala Thr Asp Val 185 180 109 Asp Asp Arg Phe Glu Thr Leu Glu Pro Glu Val Ser His Glu Glu Thr 200 205 195 112 Glu His Ser Tyr His Val Glu Glu Thr Val Ser Gln Asp Cys Asn Gln 215 115 Asp Met Glu Glu Met Met Ser Glu Gln Glu Asn Pro Asp Ser Ser Glu 235 118 Pro Val Val Glu Asp Glu Arg Leu His His Asp Thr Asp Asp Val Thr 250 121 Tyr Gln Val Tyr Glu Glu Gln Ala Val Tyr Glu Pro Leu Glu Asn Glu 260 265 124 Gly Ile Glu Ile Thr Glu Val Thr Ala Pro Pro Glu Asp Asn Pro Val 280 285 127 Glu Asp Ser Gln Val Ile Val Glu Glu Val Ser Ile Phe Pro Val Glu 295 290 130 Glu Gln Gln Glu Val Pro Pro Glu Thr Asn Arg Lys Thr Asp Asp Pro 310 315 133 Glu Gln Lys Ala Lys Val Lys Lys Lys Pro Lys Leu Leu Asn Lys 330 325 136 Phe Asp Lys Thr Ile Lys Ala Glu Leu Asp Ala Ala Glu Lys Leu Arg 345 139 Lys Arg Gly Lys Ile Glu Glu Ala Val Asn Ala Phe Lys Glu Leu Val

Input Set : A:\Rih32d31.app

Output Set: N:\CRF3\10302001\1903063.raw

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143	_	370	_				375					380				
145	Glu	Asp	Asp	Leu	Ala	Glu	Lys	Arg	Arg	Ser	Asn	Glu	Val	Leu	Arg	
	385					390					395					400
148	Ala	Ile	Glu	Thr	Tyr	Gln	Glu	Val	Ala	Ser	Leu	Pro	Asp	Val	Pro	Ala
149					405					410					415	
151	Asp	Leu	Leu	Lys	Leu	Ser	Leu	Lys		Arg	Ser	Asp	Arg		Gln	Phe
152				420		_			425	_				430	-	
	Leu	Gly		Met	Arg	Gly	Ser		Leu	Thr	Leu	Gln		Leu	Val	Gln
155	_	_,	435	_	_	1	_	440	_			-	445	T7. 1	a 1	m
	Leu		Pro	Asn	Asp	Thr		Leu	ьуs	Asn	Asp		СТА	vaı	GIÀ	TYL
158	T	450	T1_	01	3	3.00	455	7.00	7 1 a	T	T ***	460	m	Clu	C1.,	บาโ
	Leu	Leu	тте	СТА	ASP	470	ASP	ASII	Ата	пуѕ	475	vaı	TYT	GIU	Giu	480
	465 Leu	Cor	17 a 1	Thr	Dro		λen	C1 v	Dha	Δla		Val	иiс	Ψvr	Glv	
164	пец	Der	Vul	1111	485	ASII	пор	OTI	1110	490	2,5	, 41	1110	-1-	495	
	Ile	Leu	Lvs	Ala		Asn	Lvs	Ile	Ala		Ser	Ile	Pro	Tvr	-	Lvs
167			270	500	U		-1-		505					510		.
	Glu	Gly	Ile		Ser	Gly	Asp	Pro	Gly	Thr	Asp	Asp	Gly	Arg	Phe	Tyr
170	-	-	515			-	-	520	-		_	_	525	_		_
172	Phe	His	Leu	Gly	Asp	Ala	Met	Gln	Arg	Val	Gly	Asn	Lys	Glu	Ala	Tyr
173		530					535					540				
175	Lys	Trp	Tyr	Glu	Leu	Gly	His	Lys	Arg	Gly	His	Phe	Ala	Ser	Val	
	545					550					555					560
	Gln	Arg	Ser	Leu		Asn	Val	Asn	Gly		Lys	Ala	Gln	Pro		\mathtt{Trp}
179				_	565	_		_	_	570		_	_	_	575	_
	Thr	Pro	Lys		Thr	Gly	Tyr	Thr		Leu	Val	Lys	Ser		GIu	Arg
182	_	_		580	-1.	•	•	a 1	585	T	31.	17a 1	16 a.h	590	T	71-
	Asn	Trp	_	Leu	тте	Arg	Asp	600	GTĀ	ьeu	Ата	vaı	меt 605	ASP	ьуѕ	Ala
185	Lys	C1 **	595	Dho	Tou	Dro	Clu		Glu	λen	T.A11	Δrα		T.V.C	G1 v	Δen
188	_	610	Leu	FIIE	Leu	FIO	615	изъ	GIU	ASII	пец	620	GIU	Буз	OLY	ASP
	Trp		Gln	Phe	Thr	Len		Gln	Gln	Glv	Ara		Asn	Glu	Asn	Ala
	625	501	02			630				1	635	5				640
	Cys	Lvs	Gly	Ala	Pro		Thr	Cys	Thr	Leu	Leu	Glu	Lys	Phe	Pro	Glu
194	-1-		4		645	-		-		650			-		655	
196	Thr	Thr	Gly	Cys	Arg	Arg	Gly	Gln	Ile	Lys	Tyr	Ser	Ile	Met	His	Pro
197			_	660					665					670		
199	Gly	Thr	His	Val	${\tt Trp}$	Pro	His	Thr	Gly	Pro	Thr	Asn	Cys	Arg	Leu	Arg
200			675					680					685			
202	Met	His	Leu	Gly	Leu	Val		Pro	Lys	Glu	Gly		Lys	Ile	Arg	Cys
203		690					695			_		700		_		
	Ala	Asn	Glu	Thr	Arg		Trp	Glu	Glu	Gly		Val	Leu	Ile	Phe	
	705		_			710	-	_		_	715	_	_		_	720
	Asp	Ser	Phe	GLu		GLu	Val	Trp	GIn		Ala	ser	ser	Pne		ьeu
209		D1 -	-1	37- 7	725	17c 7	M	TT	D	730	T 0	mb	D	~1 ~	735	7 ~~
	Ile	ьие	тте		ASP	٧đΙ	тгр	HIS		GIU	ьец	THE	PLO		GIII	мту
212				740					745				•	750		

Input Set : A:\Rih32d31.app

Output Set: N:\CRF3\10302001\I903063.raw

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           755
215
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223 <400> SEQUENCE: 3
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226 agcatggagg acacaagaat gggaggaaag gcggactete gggaacttea ttetteacgt 180
227 ggtttatggt gattgcattg ctgggcgtct ggacatctgt agctgtcgtt tggtttgatc 240
228 ttgttgacta tgaggaagtt ctaggaaaac taggaatcta tgatgctgat ggtgatggag 300
229 attttgatgt ggatgatgcc aaagttttat taggacttaa agagagatct acttcagagc 360
230 cagcagtece gecagaagag getgageeac acaetgagee egaggageag gtteetgtgg 420
231 aggcagaacc ccagaatatc gaagatgaag caaaagaaca aattcagtcc cttctccatg 480
232 aaatggtaca cgcagaacat gttgagggag aagacttgca acaagaagat ggacccacag 540
233 gagaaccaca acaagaggat gatgagtttc ttatggcgac tgatgtagat gatagatttg 600
234 agaccctgga acctgaagta tctcatgaag aaaccgagca tagttaccac gtggaagaga 660
235 cagtttcaca agactgtaat caggatatgg aagagatgat gtctgagcag gaaaatccag 720
236 attocagtga accagtagta gaagatgaaa gattgcacca tgatacagat gatgtaacat 780
237 accaagtcta tgaggaacaa gcagtatatg aacctctaga aaatgaaggg atagaaatca 840
238 cagaagtaac tgctccccct gaggataatc ctgtagaaga ttcacaggta attgtagaag 900
239 aagtaagcat ttttcctgtg gaagaacagc aggaagtacc accagaaaca aatagaaaaa 960
240 cagatgatcc agaacaaaaa gcaaaagtta agaaaaagaa gcctaaactt ttaaataaat 1020
241 ttgataagac tattaaagct gaacttgatg ctgcagaaaa actccgtaaa aggggaaaaa 1080
242 ttgaggaagc agtgaatgca tttaaagaac tagtacgcaa ataccctcag agtccacgag 1140
243 caaqatatqq qaaqqcqcaq tqtqaqqatq atttqqctqa qaaqaqqaqa aqtaatqaqq 1200
244 tgctacgtgg agccatcgag acctaccaag aggtggccag cctacctgat gtccctgcag 1260
245 acctgctgaa gctgagtttg aagcgtcgct cagacaggca acaatttcta ggtcatatga 1320
246 gaggtteeet gettaeeetg eagagattag tteaactatt teeeaatgat aetteettaa 1380
247 aaaatgacct tggcgtggga tacctcttga taggagataa tgacaatgca aagaaagttt 1440
248 atgaagaggt gctgagtgtg acacctaatg atggctttgc taaagtccat tatggcttca 1500
249 teetqaagge acagaacaaa attgetgaga geateecata tttaaaggaa ggaatagaat 1560
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255 aaaacctgag ggaaaaaggg gactggagcc agttcacgct gtggcagcaa ggaagaagaa 1920
256 atgaaaatgo ctgcaaagga gotoctaaaa cotgtacott actagaaaag ttocoogaga 1980
257 caacaggatg cagaagagga cagatcaaat attccatcat gcaccccggg actcacgtgt 2040
258 ggccgcacac agggcccaca aactgcaggc tccgaatgca cctgggcttg gtgattccca 2100
259 aggaaggetg caagattega tgtgccaacg agaccaggac etgggaggaa ggcaaggtge 2160
260 teatetttga tgaeteettt gageaegagg tatggeagga tgeeteatet tteeggetga 2220
261 tattcatcgt ggatgtgtgg catccggaac tgacaccaca gcagagacgc agccttccag 2280
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265 <210> SEO ID NO: 4
266 <211> LENGTH: 31
267 <212> TYPE: PRT
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Input Set : A:\Rih32d31.app

Output Set: N:\CRF3\10302001\I903063.raw

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     271 <223> OTHER INFORMATION: Description of Artificial Sequence: EGF-like
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               cysteine-rich repeat
     274 <220> FEATURE:
     275 <221> NAME/KEY: VARIANT
     276 <222> LOCATION: (3)..(5)
     277 <223> OTHER INFORMATION: Wherein any Xaa may be any amino acid
     279 <220> FEATURE:
     280 <221> NAME/KEY: VARIANT
     281 <222> LOCATION: (6)..(7)
     282 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
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     285 <221> NAME/KEY: VARIANT
     286 <222> LOCATION: (10)
     287 <223> OTHER INFORMATION: Wherein Xaa is any amino acidy
     289 <220> FEATURE:
     290 <221> NAME/KEY: VARIANT
     291 <222> LOCATION: (14)
     292 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     294 <220> FEATURE:
     295 <221> NAME/KEY: VARIANT
     296 <222> LOCATION: (17)..(18)
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     305 <222> LOCATION: (29)
     306 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
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     310
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                      20
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     318 <212> TYPE: PRT
     319 <213> ORGANISM: Homo sapiens
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     325 Gly Tyr Leu Arg Lys Pro Lys Ser Met His Lys Arg Phe Phe Val Leu
     328 Arg Ala Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu
     331 Asn Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile
     332
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VERIFICATION SUMMARY

DATE: 10/30/2001

PATENT APPLICATION: US/09/903,063

TIME: 11:59:44

Input Set : A:\Rih32d31.app

Output Set: N:\CRF3\10302001\1903063.raw

L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date

L:57 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 L:60 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 L:63 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 L:309 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 L:312 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4